

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
6 May 2005 (06.05.2005)

PCT

(10) International Publication Number  
**WO 2005/040202 A2**

(51) International Patent Classification<sup>7</sup>: **C07K 7/50**,  
A61K 38/12, C07K 16/00, C07C 237/06

(21) International Application Number:  
PCT/EP2004/011719

(22) International Filing Date: 18 October 2004 (18.10.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
03023395.1 16 October 2003 (16.10.2003) EP

(71) Applicant (for all designated States except US): **APLA-  
GEN GMBH** [DE/DE]; Arnold-Sommerfeld-Ring 2,  
52499 Baesweiler (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FRANK,  
Hans-Georg** [DE/NL]; Josephina Straat 16, NL-6462  
Kerkrade (NL). **HABERL, Udo** [DE/DE]; Adenauerring  
30, 52499 Baesweiler (DE). **RYBKA, Andreas** [DE/DE];  
Heidestr. 1a, 45701 Herten (DE). **BRACHT, Franzpeter**  
[DE/DE]; Hans-Endt-Str. 117, 40593 Düsseldorf (DE).

(74) Agents: **MEYERS, Hans-Wilhelm** et al.; Postfach 10 22  
41, 50462 Köln (DE).

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.

(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished  
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: STABILIZED PEPTIDES

(57) Abstract: The present invention therefore presents modules from which helical constraints can be built by very flexible strate-  
gies. The peptide bonds involved partially compensate the hydrophobic nature of the disulfide bonds, which are also included into  
the constraint strategy. Thus, the invention presents solutions, by means of which peptide bonds or closure of disulfide bridges can  
be used alternatively for closure of the constraint. This offers greater synthetic flexibility. Moreover, the peptide bonds are more  
hydrophilic than disulfide bridges alone and offer the advantage of better solubility of the product in an aqueous surrounding. It is  
possible to attach solvation tags like glycosyl moieties, polyethylenglycol or other suitable extensions or appendices to the helical  
constraint structure. Usually, such a hydrophilic helical constraint structure replaces two hydrophobic amino acid side chains and  
thus improves pharmacologic properties of the molecule.



**WO 2005/040202 A2**